Reference: *Biol. Bull.* **181:** 72–80. (August, 1991)

Ethel Browne, Hans Spemann, and the Discovery of the Organizer Phenomenon

HOWARD M. LENHOFF

Department of Developmental and Cell Biology, University of California, Irvine, California 92717

Abstract. Ethel Browne Harvey (1885–1965) will be familiar to some as a researcher on the embryology of sea urchins. Few, however, know her as Ethel Browne who, as a graduate student, published, in 1909, a remarkable paper demonstrating for the first time the induction by a transplant of a secondary axis of polarity in the host. This process was later named "organization" by Spemann and Mangold (1924) in a paper that led to Spemann's being awarded the Nobel Prize. Why did the Nobel Committee, or other embryologists for that matter, not connect Browne's discovery with that of Spemann and Mangold? Did they consider the development of hydra as being too remote from that occurring in embryos of vertebrates? Did the 1909 paper of Ethel Browne in any way influence the thinking of Spemann or Mangold, although it was never referred to in any of Spemann's papers? In light of new information about Spemann's knowledge of Browne's work, we also can ask a number of questions about the interplay of basic prejudices in the reception accorded Browne's work.

Introduction

Ethel Browne Harvey (1885–1965) (Fig. 1) is perhaps best known to biologists for her research on sea urchin eggs, and especially for her use of the centrifuge to separate the egg into nucleated and enucleated parts. These and many of her other contributions are summarized in her classic volume, *The American* Arbacia *and Other Sea Urchins* (1956).

Long-time associates of the Marine Biological Laboratory (MBL) at Woods Hole, Massachusetts, may remember her as a summer researcher on sea urchins, as a trustee of the Laboratory, and as only the third woman to deliver a prestigious Friday Evening Lecture at the MBL, in 1944. Her husband was the Princeton physiologist, E. Newton Harvey, known for his pioneering work on bioluminescence.

Received 9 October 1990; accepted 30 April 1991.

Ethel Browne received her graduate training at Columbia University (1906–1913). While there, she was very productive, having published six papers, and was greatly influenced by T. H. Morgan and E. B. Wilson. Her dissertation, under Wilson's guidance, was a cytological study of the male gametes of the aquatic hemipteran, *Notonecta*. She participated in and initiated a number of other studies, and was a junior author on a short note about selective fertilization with T. H. Morgan (Morgan *et al.*, 1910).

Students of the biology of hydra, however, will think of Ethel Browne as the first person to demonstrate that a transplant could induce a secondary axis of polarity in a host (Browne, 1909). A similar process in amphibian embryos was later named "organization" by Spemann and Mangold (1924). The story of that work by Ethel Browne, and some unanswered questions about how her findings were received, are the subject of this paper.

The experiments reported in her remarkable 1909 paper were carried out during "the winters of 1906–1908," and in the first paragraph of that paper she acknowledges T. H. Morgan for his "kind interest and help." She then describes a series of carefully planned and executed experiments on hydra. These experiments appear homologous to the Nobel Prize experiments of Spemann and Mangold (1924), if we consider the mouth tissue of the diploblastic hydra to be developmentally like that of the lip of the blastopore of the amphibian embryo. Why did the Nobel Committee not recognize her discovery? Did it consider the hydra's development too remote from that occurring in embryos of vertebrates? Although it was never referred to in any of Spemann's papers, did the 1909 paper of

Figure 1. Ethel Browne Harvey (1885–1965). Taken in 1928; from the Archives of the Library, Marine Biological Laboratory, Woods Hole, Massachusetts.

Ethel Browne in any way influence the thinking of Spemann or Mangold? These and related questions are quite provocative in light of new information about Spemann's knowledge of Browne's work.

I will first discuss the similarities between the Nobel Prize experiments of Spemann and Mangold (1924) in which the process of embryonic induction (*i.e.* the organizer phenomenon) was demonstrated, and the 1909 work of Ethel Browne, in which she showed that a piece of hydra mouth tissue grafted to another hydra would induce the formation of a secondary axis of polarity in the recipient.

Second, I will consider newly discovered evidence showing that Spemann was aware of Browne's work long before Hilde Mangold (nee Proescholdt) began her famous organizer experiments. In addition, there is the provocative information that Mangold had worked on hydra immediately before initiating her work on amphibian embryos.

Finally, this case study raises questions about the possible interplay of basic prejudices: (1) those of medical scientists in general, and the Nobel Committee in particular, in using anthropocentric criteria when evaluating research in the biological sciences; and (2) those of male scientists in evaluating the research of female scientists, especially the work of female graduate students or of females who have no significant academic rank.

The Nobel Prize Experiment of Spemann and Mangold

Mangold's experiment involved taking a piece of the lip of the blastopore of the gastrula stage of the amphibian embryo and grafting it to the wall (flank) of another gastrula at a site distant from the host blastopore (Fig. 2). In some cases, she actually grafted the lip tissue, and in other cases simply slipped the lip tissue into the host's blastocoel. Further, to prove that the transplanted tissue actually induced changes in those of the host, Mangold took the transplant from a pigmented embryo of one species and grafted it to an unpigmented embryo of another species.

The results, of course, were remarkable and unexpected. The small piece of grafted tissue "*organized*" the tissue next to it in the host, "*inducing*" it to develop a secondary axis of polarity so that the original tissue of the host developed into two embryos rather than one (Fig. 2).

This discovery rocked the world of embryology. Hilde Mangold, in the laboratory of Hans Spemann, had shown that a piece of embryonic tissue was capable of inducing adjacent tissue to develop in a specific manner. From that moment, the search for the nature of "the organizer" was on, and for years biologists would carry out a variety of imaginative experiments, hoping to identify the organizing principle (see Hamburger, 1988). None succeeded until recently. It now appears that Melton and his associates (*e.g.*, see Ruiz i Altaba and Melton, 1989) have shown that peptide growth factors affect homeobox genes. Their findings may provide a key to understanding the elusive "organizer" in frogs.

What, then, were the experiments of Ethel Browne (1909), and how similar were they to those of Spemann and Mangold (1924)?

Key Discovery of Ethel Browne on Induction in Hydra

Ethel Browne (1909) described how the hypostomal tissue (*i.e.*, the tissue making up the mouth area of a hydra), when grafted at a certain site in the body wall of another hydra, gave "the necessary stimulus to call forth the development of a new hydranth" at that site (Fig. 3).

Although she did not use the word "organizer" in reporting her findings, her experiments describe, for the first time, the induction or "organization" of a secondary axis of polarity. Furthermore, if we consider the diploblastic,

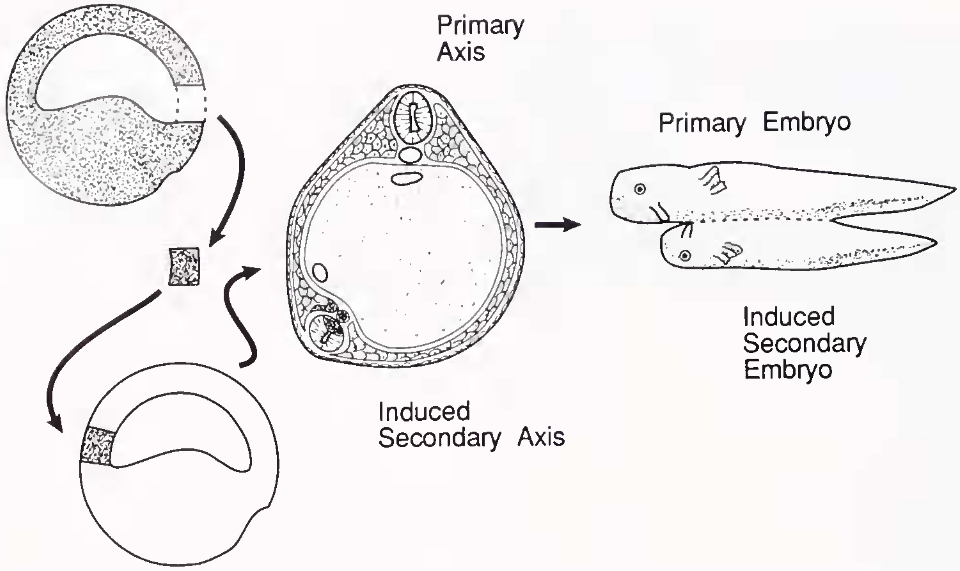


Figure 2. Mangold-Spemann transplantation experiment. Mangold removed the dorsal lip of the blastopore from a donor amphibian embryo (stippled), grafted it to the flank of a host embryo, and thereby induced a secondary axis of polarity in the host that eventually developed into a secondary embryo.

sac-like hydra as a diploblastic gastrula with a ringlet of tentacles emanating from the lips surrounding the "blastopore," her results bear a remarkable resemblance to those of the organizer experiments that Spemann and Mangold (1924) reported 15 years later using amphibian embryos.

Structure and Development of the Diploblastic Hydras

Before reviewing Browne's key experiments in detail, it is important to understand the basic structure and development of hydras. The hydra is a simple diploblastic epithelial animal made up of two cell layers—the ectoderm and endoderm—separated by a thin basal membrane called the mesoglea (Fig. 4). At one end of the animal is the "hydranth," the part involved in feeding (the capture and ingestion of prey). Between the ringlet of tentacles on the hydranth is the mouth, an opening made up of tissue called the hypostome (Fig. 4).

The hydra can reproduce asexually, by producing a bud at about the middle of its tubular body (Fig. 5A). Once

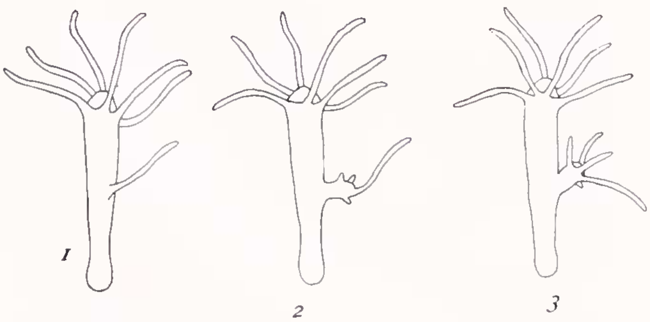


Figure 3. Browne transplantation experiment with hydra. Browne removed a piece of the hypostome (see Fig. 4) with a single tentacle (as a label) from a donor hydra, grafted it to the flank of a host hydra (#1), and thereby induced a secondary axis of polarity in the host (#2) which eventually developed into a secondary hydranth (see Fig. 4). The figures are those of Browne (1909).

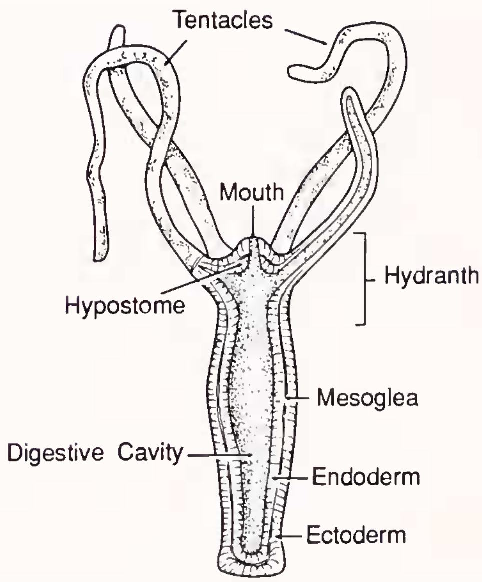


Figure 4. Diagram of a hydra illustrating its major structures.

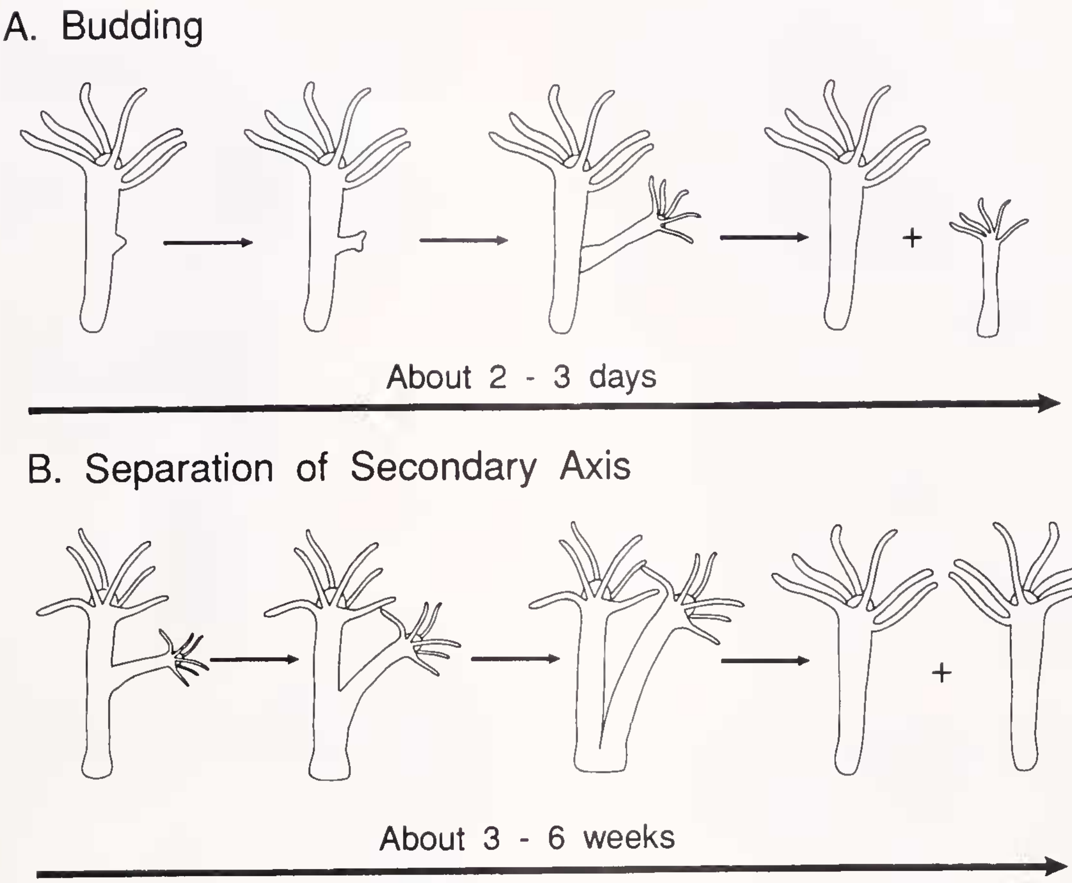


Figure 5. Difference between budding (A) and separation of a secondary axis of polarity (B) in hydra. The secondary axis of polarity can be established by the induction method of Browne described in the text, or by a kind of longitudinal fission, which can occur naturally or be initiated by cutting the upper half a hydra partway down the middle of the body column.

this bud starts to form, it will normally develop a basal disc at the point of junction between the bud and parental body tube and will detach from the parental body tube as a small, fully developed hydra within 2–3 days.

Some species of hydra are diecious; others are monecious. The gonads are usually not present when the animal is reproducing asexually by budding, and they appear at different times in different species. The zygote then develops into a miniature diploblastic hydra that is structurally homologous to a diploblastic gastrula of a number of invertebrates (Fig. 6; Brien, 1965). Note, however, that the embryo of hydra does not develop by the classically described process of the invagination of a blastula, but rather by a process similar to a delamination of cell layers (Brien, 1965).

Ethel Browne's Basic Experiments

In her first induction experiments, Browne removed a piece of the hypostome with a tentacle attached to it to serve as a marker, and grafted that tissue to various sites along the body wall of another hydra of the same species. She found that only when the hypostomal tissue (with the tentacle) was grafted to about the center of the body tube, a "new hydranth regenerated there." That new hydranth initially had one long tentacle, the one from the grafted tissue (Fig. 3).

Within a few days, this second hydranth developed a mouth and tentacles and became a secondary axis of polarity to the body of the host hydra. This new hydranth, with its accompanying body, was not a bud. Recall that a new bud develops a basal disc ("foot") and detaches from the parent stalk within 2–3 days after developing (Fig. 5A). The secondary hydranth induced in Ethel Browne's experiment, to the contrary, remained on the parental body tube for weeks before it eventually separated by a sort of longitudinal fission (*e.g.*, Fig. 5B). Browne's experiment is simple to perform; I have repeated it several times with very little difficulty.

Figure 3 shows clearly that a new hydranth was induced and that it developed a secondary axis of polarity by drawing out with it some more parental tissue. Browne asked the key question as to whether the transplanted tissue actually induced the formation of a new hydranth, or whether the cells of the transplanted tissue multiplied and then, themselves, formed the new hydranth.

To test these two possibilities, Browne devised an elegant but simple experiment involving pigmented and nonpigmented tissues. As a transplant, she used tissue taken from a green hydra the intracellular algae of which had been removed by a process described two years earlier by Whitney (1907). Normally the endodermal cells of the green *Hydra viridissima* are laden with symbiotic green algae. The host tissue in Browne's experiment was such a green hydra of the same species. Through this experiment involving the use of a piece of nonpigmented tissue transplanted to a pigmented host of the same species, Browne showed conclusively that the pigmented host tissue was organized by the nonpigmented transplant to develop into a hydranth and a secondary axis of polarity (Fig. 7).

Browne did numerous other experiments proving that it was only the hypostomal tissue (analogous to the lip of the blastopore of a gastrula) that would induce the formation of both a hydranth and a secondary axis of polarity. As she said, "it depends . . . entirely on the differentiation of the grafted material." That is to say, only the hypostomal tissue had this organizing capacity, not other tissues of hydra, such as a tentacle. Since the publication of Browne's paper (1909), a number of other investigators have used her findings in their experiments describing the developmental capacities of hydra tissues (*e.g.*, Yao, 1945; Webster and Wolpert, 1966).

Figure 7. Result of Browne's experiment in which she grafted, as donor, a piece of the hypostome and a tentacle taken from a "green" hydra whose algae had been removed, to the flank of a green hydra that still contained its endosymbiotic algae. The transplant induced a pigmented secondary axis of polarity in the host. The figure is that of Browne, 1909.

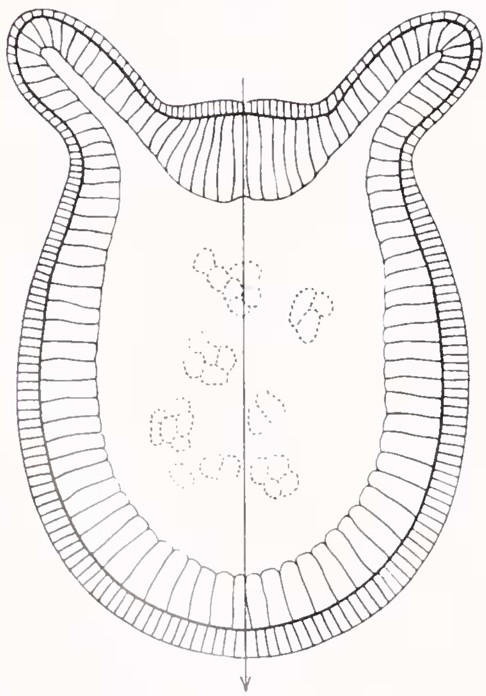
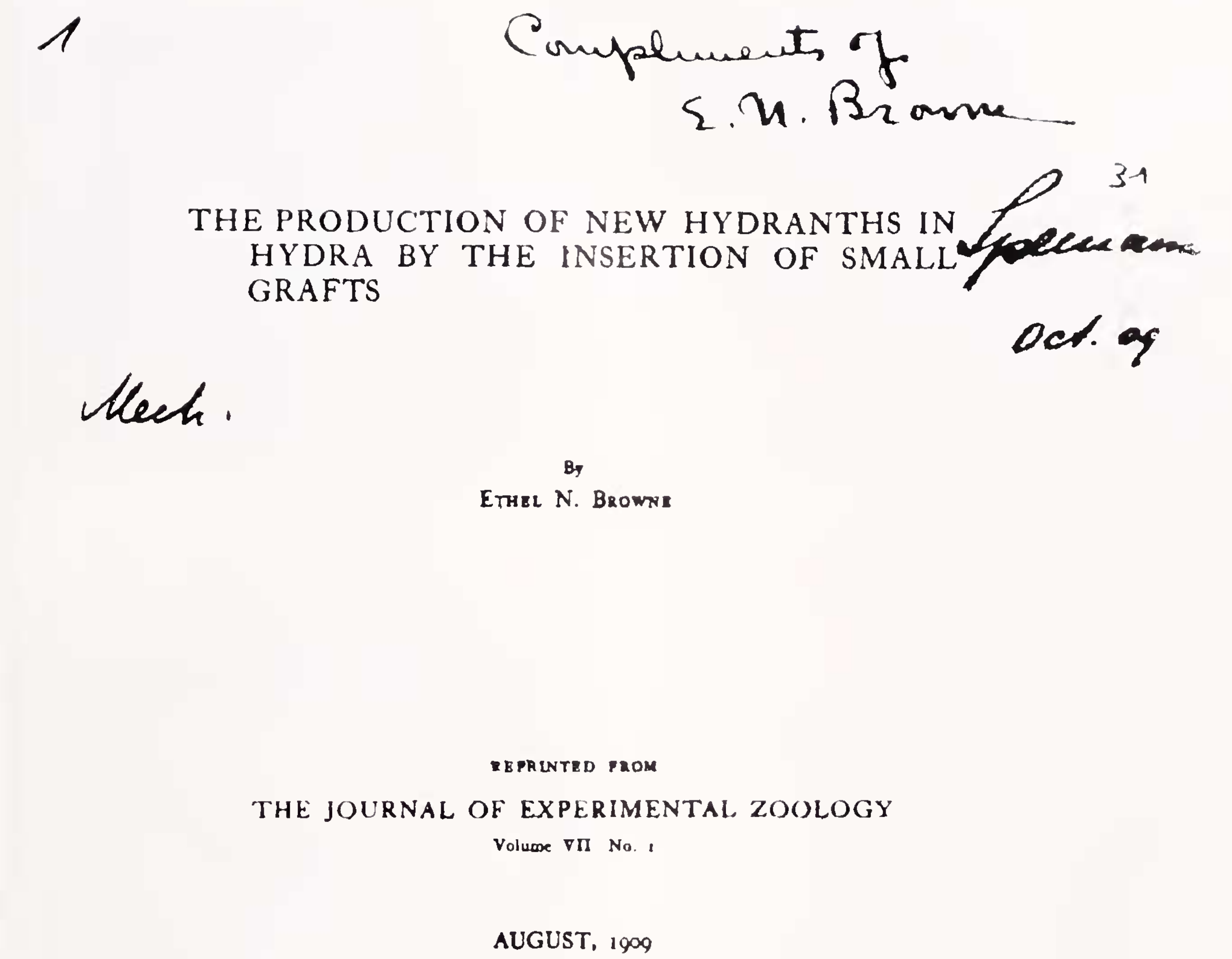


Figure 6. A young hydra just as it emerged from the embryo (Brien, 1965).

Was Either Spemann or Mangold Aware of Browne's Experiments Before Beginning Theirs?

The close analogies between the experiments of Browne (1909) and the Nobel Prize experiments of Spemann and Mangold (1924) are manifest. Both papers showed that tissue taken from specific regions of an organism or embryo, when transplanted, could organize the adjoining host tissue and induce it to form a secondary axis of polarity that is similar, in most respects, to the primary axis of polarity. But more importantly, through the use of pigmented and nonpigmented tissues, both sets of experiments proved conclusively that a true organization occurred, and not a growth and reorganization of the transplanted tissues. Browne's experiment was even more conclusive because she used pigmented and nonpigmented tissues from organisms of the same species,



1

Compliments of
E. N. Browne

31
Spemann
Oct. 09

THE PRODUCTION OF NEW HYDRANTHS IN HYDRA BY THE INSERTION OF SMALL GRAFTS

Mech.

By
Ethel N. Browne

REPRINTED FROM
THE JOURNAL OF EXPERIMENTAL ZOOLOGY
Volume VII No. 1

AUGUST, 1909

Figure 8. Cover page of reprint of Browne's 1909 paper found in Spemann's reprint collection.

whereas Spemann and Mangold (1924) used tissues taken from two different species.

Recently, in a roundabout way, I received conclusive evidence that Hans Spemann was aware of Browne's paper as early as a few months after its publication. The information came to my attention as a result of a paper on Abraham Trembley published in *Scientific American* (Lenhoff and Lenhoff, 1988). In response to that paper, we received kind letters from a number of scholars, among them Professor K. Sander of the Albert-Ludwigs-Universität in Freiberg. Professor Sander is the current Director of the University's Institute for Biology (Zoology), once directed by Spemann. In his letter (30 May 1988), Professor Sander stated that, at Spemann's suggestion, Hilde Mangold's original thesis topic was to repeat Trembley's experiment of turning hydra inside out, then following the fate of the ectoderm and endoderm in the inverted animals. Spemann, we know, was a biologist of great breadth, and, as Viktor Hamburger (1988) has noted, Spemann was aware of Trembley's famous inversion experiment and wanted to see if, after a hydra was inverted, its ectoderm would be converted to endoderm, and vice versa. Spemann apparently had no trouble in considering hydra's two cell layers as analogous to the ectoderm and endoderm of embryos. It was only after Mangold's attempts to invert hydra failed that, according to Hamburger (1988), Spemann suggested that she transplant the dorsal lip of one newt gastrula to the flank of another newt gastrula.

Responding to Sander's letter, I asked if he could find any evidence that Spemann had been aware of Browne's experiments on hydra (*i.e.*, those published in 1909). Professor Sander replied (11 July 1988) with two pages of photocopied material. The first shows the cover page of Browne's reprint found in Spemann's collection (Fig. 8). Note that the paper by Browne had a published date of

August 1909 and that Spemann, under his signed name, wrote the date "October, '09." In the upper right corner is Ethel Browne's signature after the courteous, sometimes routine, "Compliments of." Thus we know that a reprint of Ethel Browne's paper was in Spemann's possession soon after her paper was published, and that it was in his reprint collection.

From this single piece of evidence, we cannot say conclusively that Spemann read the paper first in the journal, was interested in it, and wrote (or had someone write) for a reprint. Although I find it hard to believe that, in 1909, a graduate student, on her own, would send her reprint unsolicited to a distinguished professor, that may have been the case. Perhaps because her paper dealt with the induction phenomenon, Browne may have sent the paper to Spemann unsolicited because he had published in that field earlier (Spemann, 1901). Or, because T. H. Morgan was acquainted with many European embryologists, she may have sent the paper to Spemann at Morgan's suggestion. Another scenario would be more typical: Spemann saw the paper, read it (or parts of it), and wrote to Browne for a reprint.

The other photocopied item sent to me by Professor Sander is the only page of the article having any markings (Fig. 9). Only one phrase is underlined—one containing the word "induced"—and it is accompanied by an exclamation mark in the margin. This is the only place in Browne's entire paper where she used the word "induced;" elsewhere she used such expressions as "stimulated to form." (Interestingly, she used the word "induced" regarding a case in which induction did not, and, as she proved, could not occur.) Nonetheless, even the presence of this underlining is not absolute proof that Spemann got some ideas from Browne, for we have no way of knowing with certainty whether it was Spemann himself who entered the underlining, nor when the underlining was done. But would a graduate student, postdoctoral fellow, or a visiting scholar have marked the Professor's reprint? More likely Spemann himself underlined the word "induced," for he had been working on lens induction since the turn of the century (Spemann, 1901).

As a related interpretation, one critic has suggested that Spemann may have underlined the phrase "induced to form" and entered the exclamation mark because he was peeved that Browne did not refer to his earlier work on lens induction (1901). If we accept that interpretation, then we also would have to accept that Spemann had read her paper and must have believed that Browne had truly observed a case of induction, albeit a remarkable one in which a secondary axis of polarity was induced.

From the evidence on hand, however, we can only conclude that: (1) Spemann was a man of some breadth who was familiar with the zoological, as well as the embryological literature; (2) he possessed a signed reprint of Browne's paper and received it soon after it was published; (3) someone underlined the only phrase in the paper that contained the word "induced"; (4) Spemann considered the freshwater hydra a suitable experimental system for the study of development; and (5) at his suggestion, Hilde Proescholdt (Mangold) had been working on hydra immediately before she began her research on the newt. All else remains speculation.

Was Spemann Influenced in any way by Browne's Findings?

We cannot be sure. For the sake of argument, however, let us assume that Spemann was influenced by Browne's work, and that he saw the direct link between Browne's findings and his own. If such was the case, was Spemann the sort of person who would acknowledge such a debt?

Horder and Weindling (1985, p. 204), in their article titled "Hans Spemann and the Organiser," attempt to analyze the complex nature of the man as a scientist and as an individual who had "a strong sense of nationalism." They write, "Spemann confessed in moments of humility that he was often prone to forget relevant literature which had earlier impressed him. . . ." From my limited search of the literature, I can find no reference to Ethel Browne in any of Spemann's publications (*e.g.*, Spemann, 1938).

We can get a little more insight into Spemann's personality from an interesting anecdote revealed by Viktor Hamburger in his book on *The Heritage of Experimental Embryology: Hans Spemann and the Organizer* (1988). Hamburger notes that Spemann did not put his name on papers originating from the thesis research of his graduate students, at least he did not in the cases of Hamburger and Holtfreter. With Mangold, however, Spemann not only put his name on the publication that reported the results of her thesis research, but, despite her protests (ac-

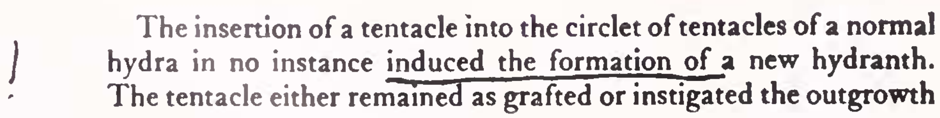

The insertion of a tentacle into the circlet of tentacles of a normal hydra in no instance induced the formation of a new hydranth. The tentacle either remained as grafted or instigated the outgrowth

Figure 9. Only excerpt showing underlining in reprint of Browne's 1909 paper found in Spemann's reprint collection.

cording to Hamburger), he even insisted on putting his name first. Some think he did the correct thing; Hamburger (1988) writes that "Spemann was perfectly right in claiming precedence . . . [because] she apparently did not fully realize the significance of her results." I could argue, however, that Mangold, who had been working on hydra just a few years earlier (Hamburger, 1988), was aware of the literature on hydra including Browne's 1909 paper, recognized the significance of Browne's experiment using pigmented and nonpigmented tissues, and, independently of Spemann, decided to conduct a similar experiment using her amphibian embryos. Mangold died in an explosion of a gasoline heater in her kitchen in 1924, the same year that her classic paper was published. She never lived to learn that her thesis work had led to a Nobel Prize.

The Nobel Prize

Mangold did not share the Nobel Prize with Spemann because the Prize is never awarded posthumously. But should not Ethel Browne have shared in the prize? I believe so; her results were essentially the same as those of Spemann and Mangold, and her published work preceded theirs by 15 years. How could the Nobel Committee have known about Ethel Browne's work if Spemann never referred to it? The usual way—by reading the literature, or by having as advisors scholars who knew the literature. But if they had read her paper, would they have recognized its significance? Probably not; most biologists of the time (and thereafter) failed to recognize the significance of Ethel Browne's extraordinary findings.

Are there other reasons why Ethel Browne's discovery was little heralded? Did the members of the Nobel Committee selecting the awardee for the prize in physiology and medicine at that time recognize primarily those discoveries that had obvious connections with human health and development? As such, was research that had some conspicuous anthropocentric connection more often recognized? Did this oversight reflect the regressive aspects of overspecialization, in that a developmental finding in an organism past the embryonic state was not considered important to embryology? (Only in recent times have we seen graduate programs and books categorized as "developmental biology," rather than as embryology alone.) Was Ethel Browne's work ignored because she was a woman with no significant station in academe?

I have presented this story to one national meeting[1] in the United States and to one international congress[2] in Great Britain. In both instances the paper polarized the audiences, even though most agreed that the experiments of Ethel Browne, like those of Hilde Proescholdt Mangold, demonstrated the phenomenon of induction of a secondary axis of polarity. Some felt that Ethel Browne's discovery was neglected, either because she was a woman graduate student, or because it was not made on a vertebrate embryo.

Opposing arguments went as follows. (1) Her work was ground-breaking, but she really did not understand the significance of her findings. (2) If she did not use the word "organizer," then she did not discover the phenomenon. (3) She was a graduate student and did what a graduate student is supposed to do: the work suggested by her mentor. (4) "I knew her for years at Woods Hole, and not once did she ever mention to me her experiments on hydra."

From reading Browne's paper closely, it seems abundantly clear that she understood the significance of her findings. In fact, if we accept the possibility that she sent her paper to Spemann unsolicited, then this would be evidence that she did understand that her findings dealt with induction. When I presented this paper in Southampton, England, Dr. Sears Crowell, a long-time researcher on hydroids at the MBL, made a comment regarding Ethel Browne Harvey that he subsequently repeated in a letter dated 3 August 1989:

> We happened to meet as she was leaving the MBL [Marine Biological Laboratory] building where she had a lab. Somewhat out of the blue she said: "You know that it was I who first discovered the organizer." Not an exact quotation. I replied that I did recognize that this was indeed the case. . . .

Ethel Browne Harvey died 2 September 1965. There is an obituary in *The Biological Bulletin* (Vol. **133:** 11). It does not mention her transplants with hydra.[3]

Acknowledgments

I thank Dr. Richard Campbell for pointing out the paper by Paul Brien to me, Dr. Klaus Sander for uncovering the reprint of Ethel Browne's paper in the collection of the late Hans Spemann, and Dr. Sears Crowell for his letter recalling his conversation with Ethel Browne Harvey. For editorial comments, I thank my colleagues at the Developmental Biology Center at the University of California, Irvine, and especially my wife and colleague,

[1] Historical Session of the American Society of Zoologists, San Francisco, California, December 1988.

[2] Historical Session of the Fifth International Congress of Coelenterate Biology, Southampton, England, July 1989.

[3] Crowell noted that the last year that Ethel Browne Harvey was listed as an investigator at the Marine Biological Laboratory was 1962. He guessed that the date of his conversation with her was in the "late summer of 1961 or 1962."

Sylvia G. Lenhoff who, like Ethel Browne, was a graduate of Goucher College of Maryland.

Literature Cited

Browne, E. 1909. The production of new hydranths in hydra by the insertion of small grafts. *J. Exp. Zool.* **7:** 1–37.

Brien, P. 1965. L'Embryogenèse et la sénescence de l'Hydre d'eau douce. *Mémoires, Académie royale Belgique, Classe des Sciences,* Tome XXXVI, Fascicule 1. Pp. 7–113. [Fig. 54 D on p. 77]

Hamburger, V. 1988. Hilde Mangold, co-discoverer of the organizer. Appendix in *The Heritage of Experimental Biology: Hans Spemann and the Organizer.* Oxford University Press, New York. Pp. xii + 198.

Harvey, E. B. 1956. *The American* Arbacia *and Other Sea Urchins.* Princeton University Press, Princeton, New Jersey. Pp. viii + 298.

Horder, T. J., and P. J. Weindling. 1985. Hans Spemann and the Organiser. Pp. 183–242 in *A History of Embryology,* Horder, T. J., J. A. Witowski, and C. C. Wylie, eds. Cambridge University Press, Cambridge. Pp. xxiv + 477.

Lenhoff, H. M., and S. G. Lenhoff. 1988. Trembley's polyps. *Sci. Am.* **256:** 108–113.

Morgan, T. H., F. Payne, and E. N. Browne. 1910. A method to test the hypothesis of selective fertilization. *Biol. Bull.* **18:** 76–78.

Ruiz i Altaba, A., and D. A. Melton. 1989. Interaction between peptide growth factors and homeobox genes in the establishment of antero-posterior polarity in frog embryos. *Nature* **341:** 33–38.

Spemann, H. 1901. Über Korrelationen in der Entwicklung des Auges. *Verh. Anat. Ges.* 15 Vers. Bonn, Pp. 61–79. (from Spemann, 1938)

Spemann, H. 1938. *Embryonic Development and Induction.* Reprinted in 1967 by Hafner Publishing Co., New York. Pp. xii + 401.

Spemann, H., and H. Mangold. 1924. Über Induktion von Embryonanlagen durch Implantation artfremder Organisatoren. *Arch. Mikr. Anat. Entw. Mech.* **100:** 599–638.

Webster, G., and L. Wolpert. 1966. Studies on pattern regulation in hydra. I. Regional differences in time required for hypostome determination. *J. Embryol. Exp. Morphol.* **16:** 91–104.

Whitney, D. D. 1907. Artificial removal of green bodies of *Hydra viridis.* *Biol. Bull.* **13:** 291–299.

Yao, T. 1945. Studies on the organizer problem in *Pelmatohydra oligactis* I. The induction potency of the implants and the nature of the induced hydranth. *J. Exp. Zool.* **21:** 147–150.